UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,739	05/26/2004	Itzhak Bentwich	050992.0302.00USCP	3738

37808 7590 02/18/2009

ROSETTA-GENOMICS
c/o PSWS
700 W. 47TH STREET
SUITE 1000
KANSAS CITY, MO 64112

EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
02/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/709,739	BENTWICH ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,31,33 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,31,33 and 35-37* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2004 and 02 January 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment after final was received and entered on 12/29/08.

Claims 26, 31, 33, and 35-37 remain pending and under consideration.

Rejections/Objections Withdrawn

The objection to the specification, and the rejection of claims 26, 31, 33, and 35-37 for lack of enablement, both for improper incorporation by reference, are withdrawn in view of Applicant's persuasive arguments submitted 12/29/08.

Specification

Applicant is required under 37 CFR 1.52(e)(5) to amend the specification to include in the paper portion all portions of Tables 1-14 that deal specifically with SEQ ID NOS: 4204050 and 117937, and in particular the portions of Tables 8 and 9 which disclose the identity of the gene or genes targeted by SEQ ID NOS: 4204050 and 117937, and the function(s) of the gene(s) as well as any related diseases. This information is deemed to be essential to making and using the invention as disclosed and will facilitate a complete examination of the application. See paragraph 213 on page 93 which indicates that the specific functions and the utilities of the oligonucleotides can be deduced from this information.

Claim Objections

Claims 31, 33, 36, and 37 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 31 is drawn to a vector comprising a nucleic acid of claim 26. However, claim 26 is drawn to an isolated nucleic acid consisting of a nucleic acid sequence. The claim uses closed language to describe the nucleic acid. As a result, claim 31 does not further limit the isolated nucleic acid set forth in claim 26, instead, it improperly adds matter which is not accounted for in claim 26, i.e. a vector. Because it does not further limit claim 26, but instead broadens it, it is an improper dependent claim. Claim 36 is objected to for the same reason. Similarly, claims 33 and 37 are objected to for similar reasons. To the extent that the recited probes consist of SEQ ID NOS: 4204050 or 117937, they do not further limit claims 26 or 35. Also, to the extent that they may comprise components not present in SEQ ID NOS: 4204050 or 117937, such as labels or further sequences, they improperly add matter which is not accounted for in claim 26 or claim 35.

Response to Arguments

Applicant's arguments filed 2/10/09 have been fully considered but they are not persuasive. Applicant argues at pages 5 and 6 of the response that claim 31 contains all of the elements of claim 26, from which it depends, and does not impermissibly expand its scope to include unrecited elements. This is incorrect. Claim 26 uses closed language to describe a nucleic acid, and claim 31 broadens claim 26 to include nucleic

acids not accounted for by claim 26. Accordingly claim 31 is an improper dependent claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 33, 36, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 31 and 36 are directed to vectors comprising a viral insert , wherein the viral insert consists of a) SEQ ID NO: 420405 or 117937, b) DNA encoding and of equal length to a), or the complement of a) or b), wherein the complement is of equal length to a) or b). The vector cannot comprise any viral insert other than the nucleic acid set forth above.

Claims 33 and 37 are directed to probes comprising a viral insert , wherein the viral insert consists of a) SEQ ID NO: 420405 or 117937, b) DNA encoding and of equal length to a), or the complement of a) or b), wherein the complement is of equal length to a) or b). The probe cannot comprise any viral insert other than the nucleic acid set forth above.

The claims as amended exclude any viral sequence of any length, other than the recited SEQ ID NOS, from the recited vectors and probes. Applicant indicates in the response filed 12/29/08 that support for the amendments is found at paragraph 35 of the specification as filed. However, a search of the specification as filed did not reveal any support for the exclusion of viral sequences from the vectors or probes of the invention. For this reason, the claims as amended recite new matter. Furthermore, the specification as filed lacks an adequate written description for the genus of vectors and probes as claimed, because it fails to adequately describe the genus of viral sequences that must be excluded, or the corresponding genus of vectors and probes that lack these sequences. In view of the multitude of viruses that exist, and the variability of sequences found in these viruses, a disclosure of a representative number of species of viral sequences would be extremely difficult to achieve. The specification as filed does not have such a disclosure. The specification as filed also does not provide any description of the distinguishing characteristics that would allow one of skill to identify a given sequence as viral or non-viral, and to then exclude such a sequence from a vector or probe. Accordingly the specification as filed fails to adequately describe the claimed genuses of vectors and probes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26 and 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ghazal et al (WO/200257437) in view of Hogan (US Pat. 5,541,308, July 30, 1996).

Ghazal taught a yeast artificial chromosome vector comprising at least a portion of a human cytomegalovirus genome, wherein the portion includes nucleotides 163187-163253, which are identical to instant SEQ ID NO: 4204050. Accordingly Ghazal taught a vector that comprised a sequence consisting of instant SEQ ID NO: 4204050.

Ghazal did not teach an isolated nucleic acid consisting of SEQ ID NO: 4204050, or a probe comprising SEQ ID NO: 4204050.

However the complete sequence of the vector insert of Ghazal comprising SEQ ID NO: 4204050 was known in the prior art at the time the invention was made. Further, the parameters and objectives for generating probes were well known in the art at the time the invention was made. For example, Hogan taught methods for generating target specific primers (col. 6-7, lines 50-67, lines 1-12), and provides extensive guidance for the selection of primers and probes. Hogan taught that "while oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 15 and about 50 bases in length" (column 10, lines 13-15). Accordingly it would have been obvious to one of ordinary skill in the art at the time of the invention to generate a probe of any

length corresponding to any fragment of the CMV genome, including the portion identical to SEQ ID NO: 4204050 disclosed by Ghazal.

Claims 35 and 37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ghazal et al (WO/200257437) in view of Buck et al (BioTechniques 27: 528-536, 1999).

Ghazal taught a yeast artificial chromosome vector comprising at least a portion of a human cytomegalovirus genome, wherein the portion includes nucleotides 163187-163253, which are identical to instant SEQ ID NO: 4204050, and which comprise instant SEQ ID NO: 117937. Accordingly Ghazal taught a vector that comprised a sequence consisting of instant SEQ ID NO: 4204050, and that comprised a sequence consisting of instant SEQ ID NO: 117937.

Ghazal did not teach an isolated nucleic acid consisting of SEQ ID NO: 117937, or a probe comprising SEQ ID NO: 117937. However, it is clear that it was obvious to those of ordinary skill in the art that sequencing primers were required in order to obtain the sequence disclosed in Ghazal, and it was of interest to amplify subsequences along the entire length of the sequence of Ghazal (see e.g. Table 1 of Ghazal). It is considered obvious for the reasons set forth below to make primers of the same length of SEQ ID NO: 117937, and further, these primers can be considered to be probes.

Buck analyzed the effect of primer design strategy on the performance of DNA sequencing primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page

530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that every single primer worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, every single control primer functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

It would have been obvious to one of ordinary skill in the art at the time of the invention to synthesize instant SEQ ID NO: 117937 as a primer in the process of determining the sequence disclosed in Ghazal. In view of the teachings of Buck, sequencing primers can be synthesized essentially anywhere along a given sequence of interest, and under optimal conditions they will reasonably be expected to perform adequately to yield sequence data. See page 533, left column, first full paragraph, and paragraph bridging pages 535 and 536. It would have been obvious to select a primer length of 22 nucleotides because those of ordinary skill normally use sequencing

primers of 19-24 nucleotides in length (see Buck abstract.). Accordingly, any 22 nucleotide fragment represented in either strand of the vector of Ghazal is considered to be obvious.

Response to Arguments

Applicant's arguments filed 12/29/08 have been fully considered but they are not persuasive.

Applicant argues that there is no way for one of skill to envisage the claimed nucleic acids within the large genus of possible probes against the sequence of Ghazal. Applicant calculates that there are at least 1,834,676 possible primers that one could arrive at using the teachings of Buck as set forth in the rejection, and at least 8,255,610 possible probes that one could arrive at using the teachings of Hogan as set forth in the rejection. However, it is the position of the Office that all of these probes and primers are equivalents for the purpose of probing or priming the sequence of Ghazal, and are therefore obvious over each other. Attention is directed to the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995) where the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties

and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties".

As noted above, the CMV sequence was well known in the art as demonstrated by Ghazal. Since the claimed oligonucleotides simply represent structural homologs of oligonucleotides suggested by the prior art as useful for sequencing or amplification primers or probes, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed oligonucleotides are *prima facie* obvious over the cited references in the absence of secondary considerations.

Applicant argues that the rejections fail to make a prima facie case of obviousness because there is nothing in the cited art to lead on of skill to select a primer or probe that is related to an miRNA, or any other sequence capable of regulating a gene transcript *in trans,* as is provided in the instant claims, from the many possible sequences. This is unpersuasive. As discussed above the possible primers and probes directed to the sequence of Ghazal are considered to be structural and functional homologs for the purpose of detecting or sequencing the sequence of Ghazal, and so are considered to be obvious over each other in the absence of secondary considerations. Applicant alleges that the claimed oligonucleotides function as or are related to miRNAs. However, this allegation does not rise to the level of a secondary consideration that would overcome the prima facie case of obviousness. finding of obviousness because it is not supported by evidence. Although the entire specification as filed is directed to the bioinformatic identification of miRNAs, there is no

evidence that the claimed sequences have miRNA or gene regulatory activity. MPEP 2144.08 makes clear that the secondary considerations sufficient to overcome a prima facie case of obviousness must be based on evidence, and that attorney arguments cannot take the place of such evidence. For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-

272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Richard Schnizer/
Primary Examiner, Art Unit 1635